

which was found to be tasteless to both tasters and non-tasters. This compound, however, is extremely insoluble, notwithstanding the hydroxy ethoxy group present. Another example was noted containing a solubilizing group and this was found to be bitter to both tasters and non-tasters. Some experiments by A. F. Blakeslee have also indicated it is due to a difference in solubility. If this is the case, however, it remains just as inexplicable why these products should be insoluble in the saliva of some individuals and soluble in others. One possible explanation, offered with no experimental proof, is that the extremely small quantity necessary to produce taste is soluble in the saliva of all individuals, while the non-tasters have in their saliva a product, possibly a protein or colloid, which precipitates this as a very insoluble product and thus causes no taste to be sensed. One argument against this hypothesis is that non-tasters can place large quantities of these products on their tongues and not experience any taste. It would seem that the excess of reagent would precipitate all available protein and would then give a sense of taste, a sort of delayed taste. This, in fact, is experienced by some people, but whether this is due to the explanation offered is not known.

Inasmuch as this phenomenon is somewhat similar in its manifestations to color blindness it has been designated taste blindness. It is admitted that there is not an exact scientific analogy but the term taste blindness so effectively describes this phenomenon its use is believed permitted.

GENETICS OF SENSORY THRESHOLDS: TASTE FOR PHENYL THIO CARBAMIDE

BY ALBERT F. BLAKESLEE

CARNEGIE INSTITUTION OF WASHINGTON, DEPARTMENT OF GENETICS, COLD SPRING HARBOR, N. Y.

Read before the Academy Tuesday, November 17, 1931

Dr. A. L. Fox¹ first showed that many people cannot detect the bitter taste in crystals of phenyl thio carbamide. In an earlier publication, Salmon and the writer² showed that inability to taste the crystals appears to be inherited as a Mendelian recessive. (The same conclusion has been reached independently by L. H. Snyder.³) In addition to "non-tasters" of the crystals, we were able to classify the "tasters" of the crystals roughly

according to their taste acuity by means of dilutions at which the bitter taste was first detected. This work on the genetics of taste thresholds has been extended, and the results on testing 103 families is presented in the present paper.

Table 1 summarizes the tests regarding "tasters" and "non-tasters." When both parents were non-tasters all the children have been non-tasters. When both parents were tasters, most of the children have been tasters but also a considerable percentage have been non-tasters. These relations would be expected if the difference between tasters and non-tasters were due to a pair of Mendelian factors. If all the tasters were heterozygous dominants one would expect a 3:1 ratio in the mating $T \times T$ and a 1:1 ratio in the back-cross $O \times T$. The deficiency in the non-taster class would be explainable by the frequent occurrence of parents homozygous for the factors for tasting. The critical mating for the hypothesis is that between two non-tasters ($O \times O$). If inability to taste the substance is due to a recessive factor, all the children should be non-tasters. Our tests from this mating furnish 22 children all of whom are non-tasters. Snyder's published results³ add 17 more, making a total of 39. So far as the tests have gone one is warranted in making certain predictions regarding parents and offspring. A taster child will have at least one parent who is a taster and all the children of two non-taster parents will be non-tasters.

TABLE 1
HEREDITY OF TASTE DEFICIENCY FOR PHENYL THIO CARBAMIDE
(Percentages in parentheses)

TYPE OF MATING	PARENTS NO. OF MATINGS	CHILDREN		TOTAL
		NON-TASTERS (O)	TASTERS (T)	
$O \times O$	10	22 (100)	0 (0)	22
$O \times T$	39	32 (43.2)	42 (56.7)	74
$T \times T$	54	22 (16.8)	109 (83.2)	131
Totals	103	76 (33.5)	151 (66.5)	227

In tables 1, 2 and 3, 6 persons were recorded as both parents and children.

The heredity differences between people in their taste perceptions of phenyl thio carbamide are not so simple as the preceding paragraph might lead one to suppose. Innate differences have been found to exist in regard to the weakest concentration (threshold) at which the substance could be detected, the apparent strength of the sensory reactions, the ability to detect differences in concentration and ability to distinguish

the taste of the thio compound from that of other substances such as acids for example.

Table 2 gives the thresholds for the families tested. The technique has been already described. Solutions were made up in artesian well water from a stock solution of 1:5000. The stock solution kept its strength without sensible deterioration for a considerable length of time. The solutions in the small bottles from which the tests were made were frequently renewed since they tended to lose their strength, perhaps on account of soluble substances on the soda fountain straws used in the test. About 0.6 cc. was usually taken up in the straw pipettes.

TABLE 2
PHENYL THIO CARBAMIDE

206	PARENTS	TASTE THRESHOLDS OF 227 CHILDREN					
TYPE OF MATINGS	NO. OF MATINGS	O	A (1:5,000)	B (1:20,000)	C (1:80,000)	D (1:320,000)	TOTALS
$O \times O$	10	22					22
$O \times A$	2	4					4
$O \times B$	8	9	1	4			14
$O \times C$	25	18		10	19	4	51
$O \times D$	4	1			2	2	5
$A \times C$	1			3	1		4
$B \times B$	5	2	1	3	2	2	10
$B \times C$	12	8			10	9	27
$B \times D$	2	2			4	4	10
$C \times C$	17	5			19	16	40
$C \times D$	12	3			10	12	25
$D \times D$	5	2		1	5	7	15
Totals	103	76	2	21	72	56	227

To avoid the psychological influence of expectation, it was a rule not to allow those about to be tested to see the test given to others. A bottle of plain water was of value at times when the subject was in doubt of his reaction or when psychological rather than taste reactions were suspected. In order to make the tests more closely comparable, all the recorded tests except two⁵ were made by the writer. The first bottle contained a 1:1,280,000 solution in which concentration none was able to detect a bitter taste. Each solution tested was four times as strong as that previously tested. The threshold was recorded as the first concentration at which the taste was distinct.

Frequently the subject would say that a certain concentration was not water but could not decide what the taste was, even when the four tastes sweet, bitter, sour and salty were suggested to him. At the next higher concentration the subject might at once call the taste bitter and sometimes say that he now knew it was a bitter taste that he had been doubtful about in the more dilute solution. In such cases the threshold

was recorded for the stronger concentration at which the subject first recognized the taste was bitter. The subject was generally given also a grade stronger than his threshold if he did not object to the bitter taste. Those who had heard about the test and therefore expected a bitter taste may have scored a lower threshold than those who knew nothing about the chemical that was being given them. Tests of a few individuals at different times of day with a series of solutions in which each was twice as strong as the one previously tested indicated that environmental factors might have some slight influence upon the tasting ability. These differences were not great, however. Greater accuracy in determining thresholds and a smoother curve of distribution would have been possible if the factor 2, or 3 instead of 4, had been used in making up the solutions. This change, however, would have doubled the number of bottles needed for a test and, although it would have been better for a laboratory experiment, it might have been too inconvenient for use in survey work among non-scientific families where the technique employed must be simplified. A larger amount of fluid at each concentration would have had similar advantages and disadvantages.

Despite the shortcomings in method, some of which have been discussed, and the relatively small numbers for a classification of this kind, it is possible to draw some definite conclusions from the data assembled in table 2. All types of matings, for which there is more than a single family represented, have given some negative children. Homozygous cannot be separated from heterozygous tasters by their thresholds, nor by the use of di ortho tolyl thio carbamide, to which some "tasters" are insensitive. In matings with *O*'s, the effect of the grades of parents upon offspring is most clearly marked. $O \times O$ as well as $O \times A$ give only *O* offspring. $O \times B$ give about half as many tasters as *O*'s. $O \times C$ give about twice as many tasters as *O*'s and $O \times D$ give about four times as many tasters as negative children. The *O* grade forms the bottom of a series not only in respect to taste acuity of the individuals but also in respect to the effect upon the proportion of negative children as well as the proportion of acute tasters in the offspring. The threshold *A* appears to behave like a *O*, but if a considerable number, instead of only 4 children, had been recorded from this mating, some tasters might have appeared among the offspring. As will be seen later, there are probably different grades even of *O*'s and, considered from the standpoint of a continuous series from *D* to *O*, it would not be surprising that, if a very large number of $O \times O$ matings were studied, they might be found to yield a few taster offspring.

The acuteness of taste among the taster children also increases with increase of taste acuity in one of the parents. Thus from $O \times B$ matings, all the tasters are *B* or poorer tasters. From the mating $O \times C$, nearly a third of the tasters are *B*'s, two-thirds *C*, and about an eighth in the most

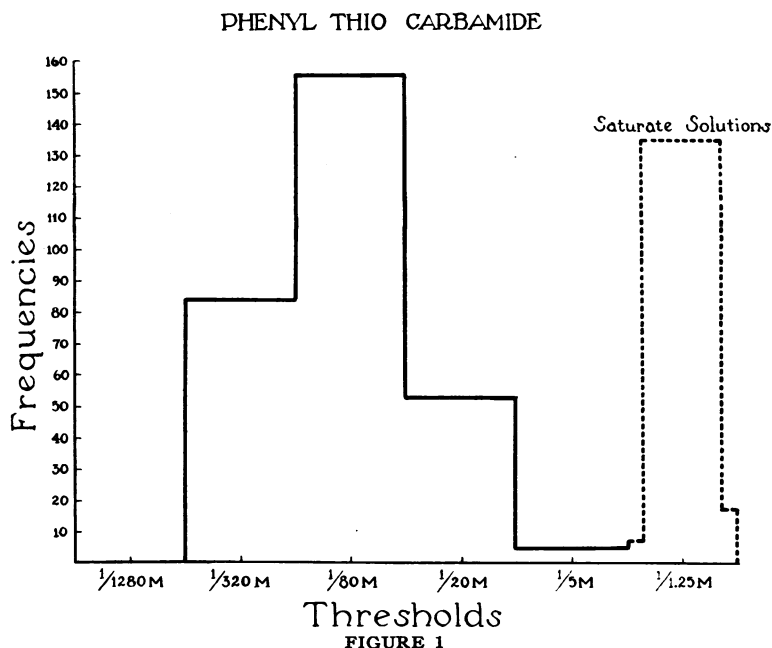
acute grade D. From the mating $O \times D$ there are no B tasters and half of the tasters belong to the acute grade D .

When both parents are tasters, the effect of their thresholds upon the grades of their offspring is not so clear. The mating $B \times B$, however, is seen to be set apart from the matings of higher grade by having a large proportion of poor tasters. The matings of higher grade all have about the same proportion of acute (D) and medium (C) tasters in their offspring. The proportion of negative offspring, however, is somewhat different. If we disregard the single mating $A \times C$, and group together the matings $B \times B$, $B \times C$ and $B \times D$ we have 35 tasters to 12 negative children; a ratio of 3:1. Taking the matings of higher grade ($C \times C$, $C \times D$ and $D \times D$) we have in the offspring 70 tasters to 10 non-tasters; a ratio of 7:1 or half as many non-tasters as from the group of lower grade parents.

In table 3 is given a summary of the threshold tests of table 2 classified under parents and children as well as according to male and female. The data suggest that more of the children than of the parents are acute tasters (grade D). This is true for both males and females. There are factors which might tend to make children score lower than their parents for the same taste acuity. Young children are not as familiar as their parents with bitter tastes. As we have pointed out earlier, familiarity with a taste will probably lead to a lower recorded threshold for the same sensation. To avoid as much as possible the difficulties of language it has been the rule not to include in the records children under 10 years of age. Older children often have difficulty in describing the taste but when asked to compare it with something they have tasted before, country children are likely to say it tastes like dandelion stems which they have stuck in their mouths in making "curls" while city children are likely to compare the taste with some medicine they have taken. The data in table 3 also suggest that there are more acute tasters among females and this difference appears in both parents and offspring. The proportions of non-tasters among males and females are reversed in parents and children and it is questionable how much significance should be attributed to apparent differences between parents and offspring and between males and females in respect to taste acuity. Age is not necessarily associated with poor taste since a subject 82 years old could detect bitterness in a 1:320,000 dilution.

The grand totals at the bottom of table 3 indicate that there is a curve of distribution with a discontinuity between the "non-tasters" (O) and those with a threshold at 1:5000. A further word is desirable at this point in regard to the manner of making the tests. A preliminary test had shown that there were few (12%) who had a threshold as high as 1:20,000. The most concentrated solution, therefore, was taken at 4

times as strong, or 1:5000. Later a few persons (1%) were found who could not taste the bitterness until the 1:5000 solution. Our practice was to try the crystals if the subject could not taste the 1:5000 solution. The fact that a few could taste bitterness in the solutions even in high (D) dilutions but were unable to taste the crystals suggested trying saturated solutions of the compound on negative subjects. The majority of non-tasters thus retested could detect bitterness in a cold saturated solution while the rest could detect it in a hot saturated solution with crystals in suspension or better in a similar hot solution in weak alcohol. Dr. Fox has found phenyl thio carbamide to be 0.26% soluble in water at



18°C. and 5.93% at 100°. In 95% alcohol it is 5.6% soluble at 16°C. and 68% in boiling alcohol. The fact that all who could not taste the crystals whom we have retested with saturated solutions have been found to be positive (25 cases) indicates that all persons can taste bitterness in the compound if only it can be gotten to the taste organs in a sufficiently concentrated condition. In a diagram (Fig. 1) we have indicated the "non-tasters," as previously defined, by a dotted line. Taste ability for the substance therefore forms a bimodal curve. The outer hump on the dotted line represents those who needed a hot saturated solution to sense the bitter taste. The inner hump represents a subject who tasted bitterness in the crystals when a large amount was taken and who had a thresh-

old of 1:5000 after chewing gum for a couple of hours. Gum chewing did not change taste of other *O*'s, however. Some *O*'s had no bitter taste from an excess of the dry crystals while some got a feeble taste under these conditions.

The fact that in the case of phenyl thio carbamide an apparent deficiency in taste has been resolved into merely a difference in thresholds suggests that threshold differences may be responsible for other apparent deficiencies in taste and smell, such as the differences in peoples' reactions to odors of Verbenas earlier discovered by the writer.⁴

TABLE 3
TASTE ACUITY FOR PHENYL THIO CARBAMIDE
(Percentages in parentheses)

	<i>O</i>	^A 1:5000	^B 1:20,000	^C 1:80,000	^D 1:320,000	TOTALS
PARENTS						
Male	26 (25.2)	3 (2.9)	16 (15.5)	48 (46.6)	10 (9.7)	103
Female	33 (32.0)	0 (0)	16 (15.5)	36 (35.0)	18 (17.5)	103
Totals, parents	59 (28.6)	3 (1.5)	32 (15.5)	84 (40.8)	28 (13.6)	206
CHILDREN						
Male	44 (41.1)	1 (0.9)	9 (8.4)	34 (31.8)	19 (17.8)	107
Female	32 (26.7)	1 (0.8)	12 (10.0)	38 (31.7)	37 (30.8)	120
Totals, children	76 (33.5)	2 (0.9)	21 (9.3)	72 (31.7)	56 (24.7)	227
Grand totals	135 (31.2)	5 (1.2)	53 (12.2)	156 (36.0)	84 (19.4)	433

The *O*'s in the tables, it may now be said, represent those who have a threshold above 1:5000. The results would be about the same if the *O*'s were defined as those who cannot taste the crystals.⁵ The factors responsible for the bimodality of the curve in figure 1 and for the fact that some who have low thresholds for bitterness in the solutions cannot taste the crystals are not entirely clear. Probably solubility of the compound in the saliva may have something to do with the phenomena. From the pH of salivas shown in table 4, it is obvious that acidity of saliva is not the controlling factor. These pH determinations were kindly made by Miss Satina by the use of brom thymol blue as an indicator. These pH's probably represent innate differences as well as possible effects of environmental factors.

The inquiry has frequently been made whether or not acuteness of taste

for the thio compound indicates acuteness of taste for other substances. This was early seen not to be the case since those in a family who were said to be the first to detect sourness in milk were sometimes good and sometimes poor tasters for the thio compound. It seemed desirable, however, to compare acuity of taste for different bitter compounds as well as for representatives of the other three primary tastes, sweet, sour and saline. Accordingly, the tests shown in table 4 were made of 21 individuals all of whom except No. 17 were connected in some way with the Department

TABLE 4
THRESHOLDS IN TASTE ACUITY

SUBJECT NO.	P. THIO CARB.	BITTER		SOUR HCl (38%)	SWEET SAC- CHARINE	SALT NaCl	ACIDITY OF SALIVA (pH)
		QUININE	PICRIC ACID				
1	0	1:5M	1:20M	1:800	1:20M	1:400	7.0
2	0	1:5M	1:20M	1:1600 ^a	1:80M	1:400	6.8
3	0	1:20M	1:20M	1:200	1:20M	1:400	6.6
4	0	1:20M	1:20M	1:400	1:10M	1:400	7.1
5	0	1:20M	1:20M	1:1600 ^a	1:20M	1:400	7.0
6	0	1:20M	1:80M	1:800	1:40M	1:400	6.8
7	0	1:20M	1:80M	1:800	1:40M	1:400	7.0
8	0	1:80M	1:80M	1:800	1:40M	1:400	6.8
9	0	1:80M	1:80M	1:1600	1:40M	1:400	6.2
10	1:20M	1:80M	1:20M	1:1600	1:40M	1:400	6.9
11	1:80M	1:5M	1:20M	1:400 ^b	1:10M	1:200 ^c	...
12	1:80M	1:5M	1:320M	1:400	1:40M	1:200 ^c	6.9
13	1:80M	1:20M	1:80M	1:1600	1:40M	1:200	7.0
14	1:80M	1:20M	1:80M	1:1600	1:80M	1:400	6.7
15	1:80M	1:20M	1:320M	1:400	1:80M	1:200	6.9
16	1:80M	1:320M	1:80M	1:1600	1:80M	1:800 ^e	7.1
17	1:80M ^d	1:320M ^d	1:80M	1:1600 ^d	1:80M
18	1:80M	1:320M	1:320M	1:1600	1:40M	1:400	6.9
19	1:80M	1:320M	1:320M	1:1600	1:80M	1:400	6.5
20	1:320M	1:20M	1:80M	1:800	1:40M	1:400	6.8
21	1:320M	1:20M	1:80M	1:1600 ^b	1:40M	1:400	6.7
Dilution							
factors	4	4	4	2	2	2	

^a All solutions of HCl taste like alum, not sour. ^b This solution of HCl tastes astringent, stronger solutions taste sour. ^c 1:200 and 1:100 NaCl taste sour and astringent. ^d Solutions of quinine, phenyl thio carbamide and HCl taste alike. ^e This solution of NaCl tastes sour, next stronger solution tastes salty.

of Genetics. The tests were made with soda fountain straws and efforts were made to avoid influence of previous tastes by taking the tests of different substances at different times or by drinking water between tests when a longer separation in time was not convenient. The method employed is somewhat crude and subject to errors already discussed in tests of the thio compound. The table gives information, however, that

appears not to have been assembled elsewhere. No one of the group is the poorest taster in respect to all the substances tested and no one is in the best grades for all the substances. Some, however, are relatively acute tasters for all substances tested and others are relatively poor for all. It was surprising further to learn that there was no close connection between ability to taste two different bitter substances. Some of these negative for the thio compound have relatively low thresholds (1:80,000) for quinine sulphate and for picric acid. Tests on a larger number might show that some who were negative for the thio compound were in the most acute grade for quinine and picric acid. The most striking difference in reaction to a bitter substance is shown by subject No. 12, who was in the poorest grade for quinine but in the most acute grade for picric acid. It had earlier been seen by the use of powdered quinine sulphate, as an attempted standard for the word bitter, that the reaction to quinine did not run parallel to that for the thio compound. Incidentally two cases were found who were apparently negative to powdered quinine sulphate. It would be interesting to test out the taste buds for different bitters.

For sour, sweet and salt test substances it was necessary to use a dilution of 2 instead of 4 to get a reasonable spread to the thresholds. Salt showed the least differences between the reactions (the highest threshold was only 4 times the concentration of the lowest) despite the differences between people in respect to the amount of salt they like in their food. The threshold at which a substance is detected does not of itself give information regarding likes or dislikes of the subject nor does it indicate the strength of sensation felt. Some were able to detect the thio compound even in the lowest concentration (1:320,000) but found little difference in sensation between this and the 1:5000 solution which is 64 times stronger. A few could not detect the compound until they were given the relatively strong solution of 1:20,000 but at this threshold made an extremely strong complaint of the bitter taste. There appears to be no close correlation between thresholds and emotional response.

The saccharine had a fleeting sweet taste at the thresholds and was difficult to record. The highest threshold was 8 times the strength of the lowest. The dry powder tastes both sweet and bitter to most subjects. For the sour hydrochloric acid the lowest threshold was 8 times as dilute as the highest. The sour sensation was easier to grade than that from saccharine and salt. Despite the recognized differences between members of a household in their ability to detect sourness in milk and also similar differences in professional milk testers, several dairy investigators who were consulted believed that no comparable tests of milk tasters had ever been made to discover how they differed in taste perceptions. The bitter substances show greater differences between the high and low thresholds than the other substances tested.

It is probable that the differences shown in table 4 represent innate heritable differences in the subjects tested, although this has been established only for the phenyl thio carbamide. By tabulating the thresholds of parents and offspring for other substances than the thio compound, it may be possible to demonstrate an hereditary basis for other taste perceptions. Certain weakly acid salts have been found tasteless to a person with a high threshold for HCl.

From the notes to table 4, it will be seen that there were some qualitative differences in reactions to the same substance, which need further study. In earlier tests, it was not infrequent to have the taste of the thio compound described by some other term than bitter, such as sour, sweet, astringent, like lemons, rhubarb, cranberries or vinegar. They have been recorded as tasters under the appropriate threshold. It has been possible as yet to retest carefully only a few of such cases. Some have been shown to be due to using the wrong term for the taste since these subjects could distinguish bitter from sour substances when they had these substances given them in comparable tests. There were several cases found, however, which were clearly due to what may be called *bitter-sour indiscrimination*. In the first (no. 17 of table 4) quinine sulphate, phenyl thio carbamide and hydrochloric acid were all described as puckery or astringent plus a taste like vinegar. Picric acid was said to have the same taste without the astringency. It will be noted that subject No. 17 detected the acid and the bitters in low concentrations although (except for the picric acid) he could not discriminate what most call bitter from what most call sour. A second subject described hydrochloric acid and the thio compound as lemony in taste but the quinine and picric acid as sour. A third, an assistant in a western department of zoölogy, was retested by a fellow assistant. She reports that quinine and hydrochloric acid are indistinguishable to her. When the solutions are strong she calls them both bitter, when they are dilute she calls them sour. Sour and bitter are terms to denote to her quantitative and not qualitative differences. Perhaps a majority of the bitter-sour indiscriminators would react like this subject and call the thio compound bitter rather than sour. It is probable therefore that a considerable number among those calling the substance bitter would be shown by tests to be examples of taste indiscrimination. There is also evidence of various grades of acuteness in taste discrimination.

A further investigation of taste indiscriminations, which appear to correspond to color blindness in vision, is deferred to a later study. Such indiscriminations in taste appear not to have been noted before. Parker in his interesting book on taste and smell⁶ makes no mention of them. A number of physiologists and psychologists who have been consulted are also unaware of mention of such phenomena in the literature. That

they have not been discovered before may be due to the fact that the emphasis has generally been placed upon the reactions of a single individual rather than upon the sensory differences between different individuals.

Differences in taste thresholds for a number of other substances than phenyl thio carbamide have been found by us and other investigators.⁷ The same is true for odors. In the single case investigated we have found these differences in powers of sensory perceptions innate and hereditary. Evidence is thus given for the belief that humans are born with innate differences in respect to all their senses and that different people live in different worlds, therefore, so far as their sensory reactions are concerned.

¹ Fox, A. L., immediately preceding paper in this issue, These PROCEEDINGS. Cf. also note in *Science News Letter*, April 18, 1931.

² Blakeslee, A. F., and Salmon, M. R., *Eugenical News*, 16, 105-108, (July, 1931).

³ Snyder, L. H., *Science, N. S.*, 74, 151-152, August 7 (1931). Dr. Snyder used para-ethoxy-phenyl-thio-carbamide, a slightly different substance from that which we used.

⁴ Blakeslee, A. F., *Science, N. S.*, 48, 298-299, September 20 (1918).

⁵ One child from the mating $C \times C$ who could not taste the 1:5000 solution had a delayed weakly bitter taste from the crystals and 2 children from the mating $O \times C$ showed a similar reaction. One parent in the $O \times O$ mating, who at first reported both solutions and crystals to be tasteless, later, after others in his family had been tested and he had heard their discussions, said the crystals tasted bitter. Other than these mentioned none could detect bitter in the crystals who did not taste bitter in the 1:5000 solution. Retests with a large amount of the crystals have given a weak bitter taste to some recorded as negative. All the parents in table 2 were tested with solutions as well as all their children except 4 children from the mating $O \times O$ who were tested with crystals. Two of the latter were tested by some one else. Otherwise all the records in the table were obtained by the writer personally. To the $O \times O$ mating might have been added 4 negative children tested with both solutions and crystals, the parents of whom were tested with crystals by the writer's assistant. The records in the tables are not entirely comparable with those in our previous paper² in which the O 's include those who tasted the solutions but found the crystals tasteless. A few errors in records in the earlier tables have been corrected.

⁶ Parker, G. H., *Smell, Taste and Allied Senses in Vertebrates*, Lippincott & Co., 1922.

⁷ Biester, Alice, Wood, Mildred W., and Wahlin, Cecile S., on sugars, *Am. J. Physiol.*, 73, 387-396 (1925). Ward, J. C., and Munch, J. C., on strychnine, *J. Am. Pharm. Assoc.*, 19, 1057-1060 (1930). Munch, J. C., on capsicums, *J. Am. Pharm. Assoc.*, 18, 1236-1246 (1929).